TEST PLAN FOR Tris (4-t-butyl-3-hydroxy-2,6-dimethylbenzyl)-s-triazine-2,4,6-(1*H*,3*H*,5*H*) trione (CAS NO. 40601-76-1)

OVERVIEW

Cytec Industries Inc. agrees to sponsor tris (4-t-butyl-3-hydroxy-2,6-dimethylbenzyl)-s-triazine-2,4,6-(1*H*,3*H*,5*H*)-trione (CAS No. 40601-76-1) in the U.S. EPA High Production Volume Chemical Program. The sponsor hereby submits a test plan for this substance. It is our intent to use existing data, plus modeling data and additional testing as proposed in the test plan to fulfill the Screening Information Set (SIDS) endpoints.

Table 1. Test Plan Matrix for tris (4-t-butyl-3-hydroxy-2,6-dimethylbenzyl)-s-triazine-2,4,6-(1*H*,3*H*,5*H*)-trione (CAS No. 40601-76-1)

CAS No. 40601-76-1	Information	Estimation	Acceptable	New Testing Required
ENDPOINT	Y/N	Y/N	Y/N	Y/N
PHYS/CHEM PROPERTIES				
Melting Point	Y	N	Y	N
Boiling Point	N	Y	Y	N
Vapor Pressure	N	Y	Y	N
Partition Coefficient	Y	Y	Y	N
Water Solubility	Y	Y	N	Y
ENVIRONMENTAL FATE				
Photodegradation	Y	Y	Y	N
Stability in Water	Y	N	Y	N
Biodegradation	Y	N	Y	N
Transport between Environmental Compartments (Fugacity)	Y	Y	Y	N
ECOTOXICITY				
Acute Toxicity to Fish	Y	N	Y	N
Acute Toxicity to Aquatic Invertebrates	Y	N	Y	N
Toxicity to Aquatic Plants	Y	Y	Y	N
TOXICOLOGICAL DATA				
Acute Toxicity	Y	N	Y	N
Repeated Dose Toxicity	Y	N	Y	N
Genetic Toxicity-Mutation	Y	N	Y	N
Genetic Toxicity-Chromosomal Aberrations	Y	N	Y	N
Toxicity to Reproduction	Y[1]	N	N	Y
Developmental Toxicity	N	N	N	Y
OTHER TOXICITY DATA				
Skin Irritation (NR)	Y	N	Y	N
Eye Irritation (NR)	Y	N	Y	N

Y = yes; N = no; NR = not required

[1] Examination of reproductive organs from 90-91 day studies

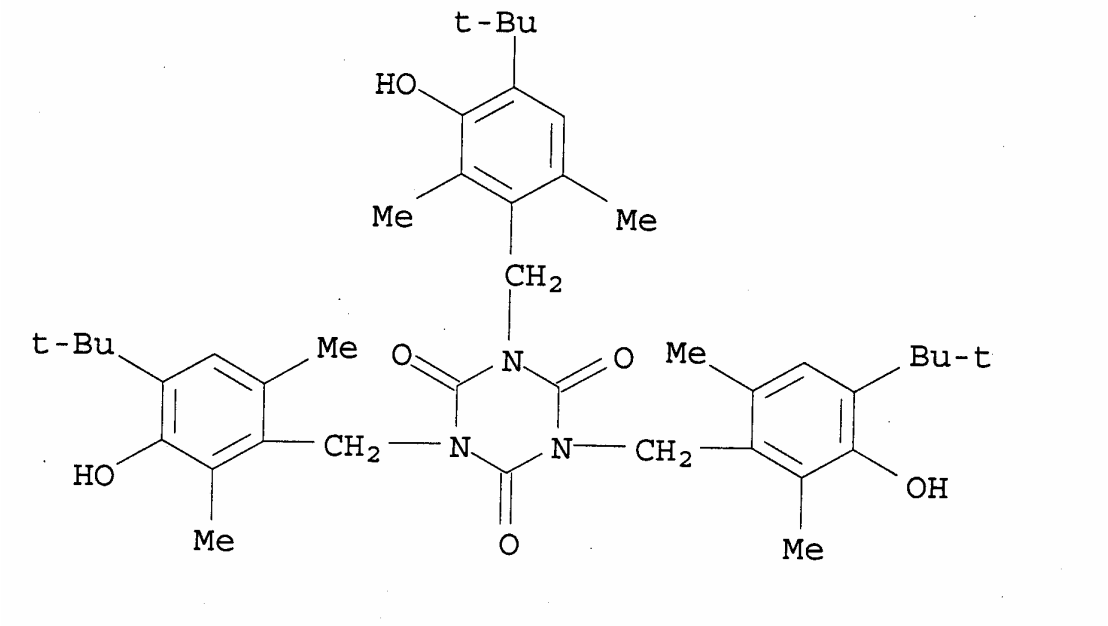
TABLE OF CONTENTS

1. Introduction

Cytec Industries Inc. has agreed to supply hazard and exposure information under The U.S. EPA High Production Volume Chemical Program for tris (4-t-butyl-3-hydroxy-2,6-dimethylbenzyl)-s-triazine-2,4,6-(1*H*,3*H*,5*H*)-trione (CAS No. 40601-76-1). This plan identifies existing data of adequate quality for this chemical, and outlines the intended testing to be conducted.

2. Designation of Test Substance

The test substance presented in this test plan is tris (4-t-butyl-3-hydroxy-2,6-dimethylbenzyl)-s-triazine-2,4,6-(1*H*,3*H*,5*H*)-trione (CAS No. 40601-76-1). It is a free-flowing white powder, with a molecular formula of C42H57N3O6. Its chemical structure is as follows:



This substance has the following synonyms:

1,3,5-tris[[4-(1,1-dimethylethyl)-3-hydroxy-2,6-dimethylphenyl]methyl]-1,3,5-triazine-2,4,6(1*H*,3*H*,5*H*)-trione
1,3,5-tris[[4-tert-butyl-3-hydroxy-2,6-xylyl]methyl]-1,3,5-triazine-2,4,6(1*H*,3*H*,5*H*)-trione
1,3,5-tris(2,6-dimethyl-3-hydroxy-4-tert-butylbenzyl) isocyanurate

It also appears as a commercial product under the Cytec Industries Inc. trade name of CYANOX® 1790 Antioxidant. According to the MSDS, the purity of this material is 93.7-98.9%.

3. General Use and Exposure Information

Tris(4-t-butyl-3-hydroxy-2,6-dimethylbenzyl)-s-triazine-2,4,6-(1H,3H,5H)-trione is produced by Cytec Industries Inc. in a closed system of reactors, centrifuges and driers. Local exhaust and dust collection are provided at the packaging stations. Under prescribed conditions of end use, which include the use of adequate ventilation and personal protective equipment, there should be minimal worker exposure. Tris(4-t-butyl-3-hydroxy-2,6-dimethylbenzyl)-s-triazine-2,4,6-(1*H*,3*H*,5*H*)-trione is an effective antioxidant for a variety of polymer systems. This substance provides superior polymer stabilization with minimal color contribution and low volatility. The substance may be used in food packaging materials and polystyrene and rubber modified polystyrene as an antioxidant. As such, it is cleared by the FDA under 21 CFR (Code of Federal Regulations) Section 178.2010. The material is also used as an antioxidant in polyethylene polymer, at the 0.05-0.10% level. The substance is melt-soluble in the polymer, and has demonstrated limited potential for migration from the polymer (Kawamura et al., 1997). The material is also used as an antioxidant in fiber (such as Spandex® PUR fiber) at the 0.5-1.5% level.

4. Criteria for Determining Adequacy of Data

All available studies were reviewed and assessed for adequacy according to the standards of Klimisch et al. (1997). Studies receiving a Klimisch rating of 1 or 2 were considered to be adequate.

5. Discussion of Available Test Information

The test plan matrix (as shown in Table 1 on page 2) was constructed after a careful evaluation of all existing data. This matrix is arranged by study type and screening data endpoints and indicates if data are provided for each end point in the sets of robust summaries.

5.1 Chemical and Physical Properties

The results of chemical/physical property testing are shown in Table 2.

Table 2. Chemical/physical properties of tris (4-t-butyl-3-hydroxy-2,6-dimethylbenzyl)-s-triazine-2,4,6-(1*H*,3*H*,5*H*)-trione

Endpoint	Value
Molecular weight grams/mol	699
Melting point	159-162 ºC
Boiling point	926 ºC*
Relative density	No data
Vapor pressure	0.000013 hPa*
Partition coefficient (Log Pow or Kow)	15.281*
Water solubility (mg/l)	2.45 E-11 mg/l*

*Estimated using EPIWIN

5.1.1 Melting Point

A melting point of 159-162 ºC is available (Cytec Industries Inc., 2001).

5.1.2 Boiling Point

EPIWIN Mpbpwin was used to estimate a boiling point of 926ºC based on the structure of the molecule and a measured melting point of 160.5ºC. The EPIWIN value is probably not accurate, since nearly all organic molecules decompose well below this temperature. Nevertheless, the high melting point, together with the EPIWIN estimate and the very large size of the molecule, which lacks functional groups known to contribute to volatility, supports the conclusion that the boiling point is very likely to be above 300ºC.

5.1.3 Vapor Pressure

No measured vapor pressure data are available for this substance. EPIWIN Mpbpwin was used to estimate a vapor pressure of approximately 0.000013 hPa, based on the structure of the molecule and a measured melting point of 160.5ºC. This estimate, combined with the observations made in Section 4.1.2 pointing to a boiling point above 300ºC, is sufficient to characterize the test substance as having a vapor pressure well below 0.001 hPa.

5.1.4 Octanol/Water Partition Coefficient

EPIWIN Kowwin has been used to estimate a log Kow of 15.281. This highly positive value is consistent with the high molecular weight, aromatic, non-polar molecular structure and is sufficient to characterize this endpoint.

5.1.5 Water Solubility

No measured water solubility data exist for the substance. EPIWIN Wskow predicts that this substance has very limited water solubility, which is consistent with the very large size of the molecule, its multiple aromatic rings and alkyl side chains (which are hydrophobic), and the absence of functional groups that would contribute significantly to water solubility. However, it would be useful to have measured water solubility data, since the aquatic studies discussed in Section 5.3 were performed with concentrations that likely exceeded the solubility limit. Therefore, water solubility testing is planned.

5.1.6 Summary/Test Plan for Physical Properties

Testing is planned to obtain a measured value for water solubility of the neat material. The data obtained from this study will be used to better predict environmental fate for the substance, and to further confirm lack of aquatic toxicity at the solubility limit.

5.2 Environmental Fate/Pathways

Results of environmental fate modeling and studies are summarized in Table 3.

Table 3. Environmental fate parameters for tris (4-t-butyl-3-hydroxy-2,6-dimethylbenzyl)-s-triazine-2,4,6-(1*H*,3*H*,5*H*)-trione

Endpoint	Value
Indirect Photolysis (OH sensitizer) (Hydroxyl Radical Rate Constant)* (Atmospheric $T_{1/2}$)*	 9.08947 E-11 cm^3/molecule-sec 1.4 hours
Stability in Water*	$T_{1/2}$ > 1 year
Henry's Law Constant*	1.7E-27 atm-m^3/mol
Koc*	1E+10
Bioconcentration Factor (log BCF)*	0.500
Environmental transport (Fugacity Level III mass percentages)*	Air = 0 Water = 1.28 Soil = 31.6 Sediment = 67.1
Biodegradation	25.9% biodegraded in 28 days (not readily biodegraded)

* Estimated using EPIWIN

5.2.1 Photodegradation

Photodegradation with hydroxyl radical sensitizer was estimated using EPIWIN/Aop (v1.90). An overall hydroxyl radical rate constant of 9.08947 E-11 cm^3/(molecule*sec) was calculated based on the summation of individual rate constants for each bond fragment in the molecule using the program algorithm. A half-life of 1.4 hours was calculated assuming a constant concentration of OH radical and pseudo first order kinetics. Atmospheric photodegradation is not expected to be a significant elimination pathway, since this substance has limited volatility.

5.2.2 Stability in Water

EPIWIN Hydrowin predicts that the rate of hydrolysis of the material in neutral water at ambient temperatures will be extremely slow, with a half life of > 1 year. This estimate is based on the presence of urea functional groups in the molecule. No other functional groups in the molecule (including the phenolic function) are expected to be subject to hydrolysis. In addition, the very limited water solubility of this substance further reduces the potential for hydrolysis.

5.2.3 Fugacity

Level III fugacity modeling has been conducted on the test material using the EPIWIN model. Inputs to the program are CAS No. 40601-76-1 and a melting point of 161 ºC. Emission rates inputted into the program were air: 0 kg/hr, water: 1,000 kg/hr, soil: 1,000 kg/hr and sediment: 0 kg/hr. The following half-lives were calculated: T ½ air = 2.82 hr, water = 3,600 hr, soil = 3,600 hr, and sediment = 14,400 hr. A Henry's Law Constant of 1.7E-0027 atm-m^3/mol and a soil sediment partition constant (Koc) of 1E+10 were estimated using the EPIWIN/Henry and

Pckoc Programs, respectively. The percent mass balances predicted for this substance in air, water, soil and sediment are shown in Table 3. As shown, the majority of the material partitions to soil and sediment.

5.2.4 Biodegradation

Results of an OECD Test Guideline 301 B, Ready Biodegradability: Modified Sturm Test (CO2 evolution) show that Cyanox 1790 is biodegraded to some extent by wastewater bacteria (25.9% after 28 days), but is not readily biodegraded (Baldwin, 2002). This test was assigned a reliability rating of 2, and is considered to be adequate. However, it is possible that this test underestimates the ability of the material to biodegrade since the concentration used was toxic to the bacteria and greater than the solubility limit.

5.2.5 Bioconcentration

A bioconcentration factor was calculated using the EPIWIN BCF Program (log BCF = 0.5).

5.2.6 Summary/Test Plan for Environmental Fate Parameters

Estimated values are available for the hydroxyl radical induced photolysis rate constant and atmospheric half-life, Henry's Law Constant, soil sediment partition coefficient, Fugacity Level III environmental transport parameters and bioconcentration factor. No further testing is planned for these endpoints. No testing is planned for water stability (hydrolysis) because this material does not have functional groups known to be easily hydrolyzed under neutral ambient conditions and has very limited solubility in water. The existing biodegradation study is considered to be adequate; therefore no additional biodegradation studies are planned.

5.3 Ecotoxicity

Tris (4-t-butyl-3-hydroxy-2,6-dimethylbenzyl)-s-triazine-2,4,6-(1*H*,3*H*,5*H*)-trione is not expected to be a hazard to aquatic species, since the material has very limited estimated water solubility (2.425 E^{-11} mg/l). Therefore, aquatic toxicity testing for this material is not considered to be relevant. Nevertheless, studies have been performed in fish and Daphnia to characterize the toxicity of the material at its solubility limit.

5.3.1 Acute Toxicity to Fish

A static OECD Test Guideline 203 limit study in juvenile rainbow trout was performed with Cyanox 1790 (Glover, 2002a). The no observable effect concentration (NOEC) and lethal concentration in 50% of the organisms (LC_{50}) in this 96-hour study were 100 and > 100 mg/l, respectively. None of the fish exposed to the highest concentration tested (100 mg/l) died or exhibited signs of toxicity by 96 hours. This study was given a reliability rating of 2 (valid with restrictions) since concentrations of test material were not analytically confirmed. In this study, the actual concentration used was the amount of material that remained in solution after the mixture containing 100 mg/l was filtered. Therefore, the concentration that was used was actually the solubility limit of the test material in the medium at 15 degrees C. EPIWIN modeling predicts a solubility in water at 25 °C of 2.425 E^{-11} mg/l. Accordingly, the actual

concentration of material that the rainbow trout were exposed to in the OECD study approximates this value. Since the material was not toxic to rainbow trout at the solubility limit, it is not expected to be toxic to fish at environmentally relevant concentrations.

5.3.2 Acute Toxicity to Aquatic Invertebrates

A static OECD Test Guideline 202 limit study in Daphnia was performed with Cyanox 1790 (Glover, 2002b). The no observable effect concentration (NOEC) and lethal concentration in 50% of the organisms (LC_{50}) in this 48-hour study were 1000 and > 1000 mg/l, respectively. In this study, 10% of the organisms exposed to the highest concentration tested (1000 mg/l) died by 48 hours. Since the mortality rate in the controls also was 10%, the deaths of Daphnia exposed to the test material were not considered to be treatment-related. This study was given a reliability rating of 2 (valid with restrictions) since concentrations of test material were not analytically confirmed. In this study, the actual concentration used was the amount of material that remained in solution after the mixture containing 1000 mg/l was filtered. Therefore, the concentration that was used was actually the solubility limit of the test material in the medium at 20 degrees C. As mentioned previously, EPIWIN modeling predicts a solubility in water at 25 °C of 2.425 E^{-11} mg/l. Accordingly, the actual concentration of material that the Daphnia were exposed to in the OECD study approximates this value. Since the material was not toxic to Daphnia magna at the solubility limit, it is not expected to be toxic to aquatic invertebrates at environmentally relevant concentrations.

5.3.3 Acute Toxicity to Aquatic Plants

Testing for toxicity to aquatic plants has not been performed. However, it is believed that no testing is necessary, since the material appears to be virtually insoluble in water and the EC50 value for algal toxicity predicted by EPIWIN modeling (6.14E^{-10} mg/l) is higher than the predicted solubility limit. If results of the proposed water solubility test indicate that the material is soluble in water, an algal toxicity test will be performed.

5.3.4 Summary/Test Plan for Ecotoxicity

Results of adequate studies in rainbow trout and Daphnia magna show that tris (4-t-butyl-3-hydroxy-2,6-dimethylbenzyl)-s-triazine-2,4,6-(1*H*,3*H*,5*H*)-trione is not toxic to these species at the solubility limit. EPIWIN modeling predicts an EC50 value for algae that is higher than the predicted solubility limit. Algal toxicity testing will be conducted if the proposed water solubility test indicates a value significantly greater than the predicted value.

5.4 Human Health Data

5.4.1 Acute Mammalian Toxicity

This endpoint is filled by a sufficient oral toxicity study in rats and an additional dermal study in rabbits (Carpenter, 1973). The oral and dermal LD_{50} values (lethal doses in 50% of the animals) for Cyanox 1790 were greater than the highest dose tested (10,000 and 5,000 mg/kg, respectively). These concentrations also did not cause any signs of toxicity. The LC_{50} value for

aerosol inhalation in a poorly described study was also greater than the highest dose tested (20 mg/l).

5.4.2 Repeated Dose Mammalian Toxicity

Sufficient oral, repeated dose toxicity tests have been conducted in both rats and dogs. The results are summarized in Table 4.

Table 4. Repeated Dose Toxicity of Cyanox 1790

Species/ Exposure	Dose[a] (deaths)	Gross Changes	Histopathological Changes	Clin. Chem/Hemat. Changes
SD rat, 90 days, oral feed (Miller, 1977a)	25 (0) 100 (1) 400 (0)[b]	alopecia, diarrhea, encrustment around nares same as above same as above	none none mononuclear leukocyte infiltration in the liver (N = 1)	none ↑rbc, ↓ glucose ↓ glucose, ↑ GGTP
Beagle dog, 91 days, oral feed (Miller, 1977b)	7.5 (0) 15 (0) 30 (0)[b]	soft stool, ↓ bw (females) same as above same as above	none none none	↓ glucose, GOT ↓ glucose, rbc ↓ glucose, GOT
Beagle dog, 91 days, oral feed (Procter et al., 1983)	46 (0)[b]	↓ food in females	none	none
SD rat, 30 days, oral feed (McElroy and Ward, 1976)	0.5 % (0) 1.0 % (0)[b] 2.0 % (0)[c]	diarrhea, skin irritation diarrhea, skin irritation. ↑ food , ↓ bw (females)	none none changes in liver (N = 1 male)	not determined not determined not determined
Beagle dog, 30 days, oral feed (Upman and Ward, 1976)[d]	25-84 (0) 100 - 333 (0) 400[c] - 1335 (0) 1600 (0)	soft feces soft feces soft feces, ↓ bw, food, ↑ kidney wt. soft feces, ↓ bw, food , ↑ liver, kidney, adrenal wt.	mild - moderate changes in liver marked changes in liver marked changes in liver marked changes in liver	not determined not determined not determined not determined

GGTP = gamma-glutamyl transpeptidase; GOT= glutamic-oxaloacetic transaminase
[a] Dose is in mg/kg unless listed otherwise; [b] No effect level assigned to study; [c] Low effect level assigned to study;
[d] Study was assigned a reliability rating of 4 (not assignable)

Ninety or ninety-one day feeding studies have been conducted with Cyanox 1790 in rats and dogs. The no observable effect levels in these studies were greater than the highest doses tested (400 and 46 mg/kg/day, respectively). Clinical signs such as diarrhea, soft stools, or encrustment of the nares were noted in some animals treated with the test material. Study personnel attributed these signs to ingestion of a powdered food and did not consider them to be related to test material. The clinical chemistry findings in rats and dogs treated with Cyanox 1790 for 90-91 days (ie. elevated gamma-glutamyl transpeptidase in high dose male rats, decreased glutamic-oxaloacetic transaminase in female dogs, decreased glucose in female rats and male and female

dogs, increased red blood cell counts in mid-dose male rats and decreased red blood cell counts in male dogs) were not considered to be related to test material since they were not dose-dependent and were within normal limits. Study personnel also did not consider the reduced body weight gains in female dogs treated for 90 days with 7.5, 15 or 30 mg/kg/day to be related to test material because 1) food consumption was comparable between groups and 2) no abnormal clinical signs were noted. Reduced food consumption in female dogs treated with 46 mg/kg/day test material for 90 days also was not considered to be relevant since no other effects were noted.

Results of a 30 day feeding study in rats indicate that dietary administration of up to 1.0% Cyanox 1790 (1,190 mg/kg/day in females and 1,200 mg/kg/day in males) had no adverse effects on food consumption, body weight, weight of liver or kidneys, or gross pathology of internal organs. A concentration of 2% (2,380 mg/kg/day in females and 2,480 mg/kg/day in males) was associated with decreased body weight and increased food consumption in females.

In a 30-day study in beagle dogs, administration of up to 1,600 mg/kg/day was not associated with increased lethality. Concentrations of test material ≥ 100 mg/kg/day were associated with marked histopathological changes in the liver. The dose at which liver toxicity was first noted is difficult to determine due to the fact that higher concentrations of test material than desired were administered to the animals during the latter part of the study. The lowest observable effect level assigned by study personnel was 400 mg/kg/day. However, since all doses appeared to cause histological changes in the liver, the LOAEL appears to be lower than the lowest dose tested (25 mg/kg for 3 weeks, followed by 84 mg/kg for 9 days).

5.4.3 Genetic Toxicity

5.4.3.1 Mutagenicity

Tris (4-t-butyl-3-hydroxy-2,6-dimethylbenzyl)-s-triazine-2,4,6-(1*H*,3*H*,5*H*)-trione has been tested for mutagenicity in an OECD Test Guideline 471 (bacterial mutagenicity) study conducted with *S. typhimurium* strains TA98, TA100, TA1535, TA1537 and E. coli strain WP2uvra- (Krul and Ommen, 2001), and in an OECD Test Guideline 476 (mammalian cell mutagenicity) study conducted with cultured mouse lymphoma L5178Y cells (Steenwinkel, 2001). Results of both tests were negative.

5.4.3.2 Chromosomal aberration

A mouse micronucleus study has been conducted according to GLP with concentrations of tris (4-t-butyl-3-hydroxy-2,6-dimethylbenzyl)-s-triazine-2,4,6-(1*H*,3*H*,5*H*)-trione up to 5,000 mg/kg (Guenard, 1983). In this test, there was no significant difference between the numbers of micronucleated polychromatic (PCE) or normochromatic erythrocytes (NCE) in treated animals versus vehicle-treated controls.

The material also has been tested for its ability to cause chromosomal aberrations in an OECD Test Guideline 473 study performed with cultured Chinese Hamster Ovary Cells (CHO K-1 line) (deVogel, 2001). In two separate tests, there was no significant effect of the test material on the number of cells with aberrations (with and without metabolic activation). In both of the tests, the

highest concentration of test material used (250 micrograms/ml) did not cause the desired degree of inhibition of the mitotic index (50-70%). However, higher concentrations could not be tested due to insolubility.

5.4.4 Reproductive and Developmental Toxicity

No reproductive or developmental toxicity tests with tris(4-t-butyl-3-hydroxy-2,6-dimethylbenzyl)-s-triazine- 2,4,6-(1*H*,3*H*,5*H*)-trione have been performed. However, results of the ninety or ninety one day, repeated dose oral studies in rats and dogs indicate that the material has no effect on histopathology of male (prostate, testes, epididymides or seminal vesicle) or female (uterus, ovaries, or vagina) reproductive organs at concentrations up to 400 mg/kg/day and 46 mg/kg/day, respectively (Miller, 1977b; Procter et al., 1983). These studies are not considered to be sufficient to characterize the effect of the material on fertility, since no systemic toxicity was noted at the doses administered and the doses were lower than the limit dose recommended by the OECD (1000 mg/kg/day). Since the effect of the material on development also has not been assessed, testing is planned for both endpoints (OECD Test Guideline 421).

5.4.5 Additional Data

5.4.5.1 Skin and Eye Irritation

Results of a modified Draize-Shelanski Repeat Insult Patch Test in humans show that administration of 2.5% Cyanox 1790 in petrolatum is not irritating to skin (Kligman, 1976). Administration of 100 mg solid test material also is not irritating to rabbit eyes (Carpenter, 1973).

5.4.5.2 Sensitization

Results of a modified Draize-Shelanski Repeat Insult Patch Test conducted in one hundred healthy adults indicate that 2.5% Cyanox 1790 in petrolatum is not sensitizing to human skin (Kligman, 1976).

5.4.6 Summary/Test Plan for Mammalian Toxicity

Adequate studies with tris(4-t-butyl-3-hydroxy-2,6- dimethylbenzyl)-s-triazine- 2,4,6-(1*H*,3*H*,5*H*)-trione have been conducted for all endpoints except reproductive and developmental toxicity. Acute oral, inhalation and dermal studies show that acute exposure to fairly large amounts of the material is required to cause lethality or symptoms of toxicity. The material is not irritating to eyes or skin, and is not sensitizing. Results of an adequate 30-day repeated dose study in rats show that dietary exposure of up to approximately 1,100 mg/kg/day does not cause toxicity to rats. Adequate studies in vivo and in vitro show that tris(4-t-butyl-3-hydroxy-2,6- dimethylbenzyl)-s-triazine- 2,4,6-(1*H*,3*H*,5*H*)-trione is not mutagenic or clastogenic.

Since the highest dose administered in the 90-day repeated dose studies in rats and dogs was not sufficient to cause systemic toxicity and was not a limit dose, this study cannot be used to fill the reproductive toxicity endpoint. An OECD Test Guideline 421 (reproduction/ developmental

toxicity screening) study will be performed to fill both the reproductive and developmental toxicity endpoints. The material will be given by the dietary route since this route of administration was used for all of the previously conducted repeated dose toxicity studies.

6. Summary

Physical properties

Adequate data are available for melting point, boiling point, vapor pressure and partition coefficient. Water solubility testing is planned to obtain a measured value, which will be used to further predict environmental fate, and support the lack of aquatic toxicity at the solubility limit.

Environmental fate properties

EPIWIN modeling provides adequate data for hydroxyl radical induced atmospheric photodegradation and environmental transport, as well as bioconcentration factor and Henry's Law Constant. No testing is planned for water stability (hydrolysis) because this material does not have functional groups known to be easily hydrolyzed under neutral ambient conditions, and because this substance has very limited solubility in water. Since the biodegradation study is considered to be adequate, no additional testing for this endpoint is planned.

Aquatic toxicity

Tests that have been performed with rainbow trout and Daphnia indicate that the material is not toxic to these species at the highest obtainable dissolved concentration. Since the estimated water solubility of the material is extremely low and the ECOSAR-estimated EC_{50} value is greater than this value, the material would not be expected to be toxic to algae at environmentally relevant concentrations. Therefore, no testing in algae is necessary.

Mammalian toxicity

Adequate tests have been performed for all mammalian toxicity endpoints except reproductive and developmental toxicity. An OECD Test Guideline 421 study will be conducted by the dietary route to fill the reproductive and developmental toxicity endpoints.

7. References

Baldwin KL. 2002. CT-741-02. Ready biodegradability: CO2 evolution (modified Sturm Test). Toxicon Corporation Study Number 02J0014c for Cytec Industries Inc., dated July 23.

Carpenter CP. 1973. Antioxidant A-1790, Range finding toxicity tests: single oral, single dermal, eye irritation (FHSA). Carnegie-Mellon University Report for American Cyanamid Company, dated September 17, 1973.

Cytec Industries Inc. 2001. Material safety data sheet for Cyanox 1790 antioxidant, dated 5/29/2001.

deVogel N. 2001. Chromosomal aberration assay with Cyanox 1790 antioxidant in cultured Chinese hamster ovary cells. TNO Nutrition and Food Research, Netherlands Organization for

Applied Scientific Research Project 010.45007/01.02 for Cytec Industries BV, dated April 11, 2001.

Glover S. 2002a. CT-741-02. Acute toxicity to rainbow trout, Oncorhynchus mykiss, under static test conditions. Toxicon Corporation Study Number 02J0014d for Cytec Industries Inc., dated May 14.

Glover S. 2002b. CT-741-02. Acute toxicity to the water flea, Daphnia magna, under static test conditions. Toxicon Corporation Study Number 02J0014a for Cytec Industries Inc., dated July 22.

Guenard J. 1983. Project 014894. Mouse micronucleus assay with Cyanox 1790. RCC Research and Consulting Company, Ltd., Itingen Switzerland, Report for American Cyanamid Company, dated Jun 1.

Kawamura Y, Miura M, Sugita T and Yamada T. 1997. Residue and release of antioxidants and ultraviolet stabilizers in polyethylene products in contact with foodstuffs. J Food Hyg Soc Japan 38(1):27-33 [Japanese].

Kligman AM. 1976. Modified Draize-Shelanski Repeat Insult Patch Test for Antioxidant A-1790. BB Project Number 533-2077 for American Cyanamid Company dated August 9, 1976.

Krul C and van Ommen B. 2001. Bacterial reverse mutation test with Cyanox 1790 antioxidant. TNO Nutrition and Food Research, Netherlands Organization for Applied Scientific Research Project 010.45007/01.01 for Cytec Industries BV, dated May 16, 2001.

McElroy KE and Ward CO. 1976. Cyanox 1790 antioxidant: Thirty-day feeding to rats. Huntingdon Research Center Report No R6246-11 (Study 1-349) for American Cyanamid Company, dated October 6, 1976.

Miller TJ. 1977a. Cyanox 1790 antioxidant: Ninety-day feeding to rats. Huntingdon Research Center Report No R1126-289 for American Cyanamid Company, dated May 16, 1977.

Miller TJ. 1977b. Cyanox 1790 antioxidant: Ninety-day feeding to dogs. Huntingdon Research Center Report No N11276-289 (study 1-273N) for American Cyanamid Company, dated May 18, 1977.

Procter B et al. 1983. A 13-week oral toxicity study (dietary) of CL 226,034 in the beagle dog. Bio-Research Laboratories Ltd. Project No 81512 for Cyanamid Canada, Inc., dated August 22, 1983.

Steenwinkel M-JST. 2001. Gene mutation test at the TK-locus of L5178Y cells with Cyanox 1790 antioxidant. TNO Nutrition and Food Research, Netherlands Organization for Applied Scientific Research Project 010.44003/01.02 for Cytec Industries BV, dated May 16, 2001.

Upman PJ and Ward CO. 1976. Cyanox 1790 antioxidant: Thirty-day feeding to dogs. Huntingdon Research Center Report No 6246-112 for American Cyanamid Company, dated August 23, 1976.